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Pre-dialysis kidney function and its rate of decline predict mortality and hospitalizations after starting dialysis

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Abstract

Objective: To determine if kidney function level and its rate of decline in the immediate pre-dialysis period among veterans transitioning to end-stage renal disease (ESRD) predicts post-dialysis mortality and hospitalization.

Patients and Methods: In 19,985 veterans transitioning to ESRD during 10/1/2007–03/30/2014, we examined kidney function and its slope over the final year of the prelude period. Two categories of low versus high estimated glomerular filtration rate (eGFR, dichotomized at 10 mL/min/1.73m^2) and slow versus fast slope (dichotomized at −10 mL/min/1.73m^2/year) were combined into four groups. Their associations with 12-month post-ESRD all-cause and cardiovascular (CV) mortality and hospitalization rates were examined in adjusted models accounting for clinical characteristics and laboratory measurements at transition.

Results: Patients, 66±11 years old, and 34% blacks, had a median[IQR] eGFR at transition and slope of 9.7[7.1,13.3] mL/min/1.73m^2 and −10.5[−18.8,−5.9] mL/min/1.73m^2/year, respectively. Patients with a low eGFR and slow slope, had the lowest risk of 12-month all-cause and CV

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mortality, and hospitalization rate. Conversely, patients with high eGFR and fast slope had the highest risk of all-cause and CV mortality and hospitalization rate compared to patients with a low eGFR and slow slope. This relationship persisted in sensitivity analyses, including propensity scoring.

Conclusions: A kidney profile of a low eGFR and slow slope in the prelude period is associated with favorable early dialysis outcomes in veteran patients. Trials to examine a more conservative approach to dialysis are warranted.

Keywords

Conservative management; transition of care in CKD; prelude; vintage; mortality; hospitalization; estimated glomerular filtration rate; disease progression; veterans

Introduction

Over 120,000 persons transition to end-stage renal disease (ESRD) each year in the US, mostly with dialysis.[1,2]Mortality rates for dialysis patients are especially high in the first months after transition and a study investigating nursing home patients suggested that functionality in this early post-transition period was also substantially reduced.[2,3] Thus, discussions have emerged pertaining to the benefit of early initiation of dialysis therapy in older persons, especially those with slower progressing kidney disease. Ironically, estimated glomerular filtration rate (eGFR) at the time of transition has progressively become higher, indicating a trend toward earlier transition, or a more aggressive dialysis initiation. As of 2014, the US average eGFR at initiation was 10.2 mL/min/1.73m[2].[1] Despite these trends, the optimal timing of ESRD transition still remains controversial. Although some studies and clinical guidelines have previously suggested that early initiation may be beneficial,[4–9] a clinical trial and other observational studies have suggested otherwise.[10–15] However, many of the latter studies were limited in data on the rate of disease progression and laboratory measures from the period prior to transition, which are important drivers of eGFR levels at transition.[16] As single eGFR and its slopes have become more readily available in clinical practice,[17] it may be of importance to examine the use of both metrics in risk prediction.

In addition to the controversy of ESRD timing in the US population, it is uncertain if this is externally valid for the US veteran population. The veteran population comprise of predominately older males with likely different ailments compared to that of the greater US population. Preliminary data from United States Renal Data System (USRDS) “Transition-of-Care-in-CKD” Special Study Center have shown that 11% of incident US ESRD patients each year are veterans, and that high mortality rates in the first months after transition also exist in this veteran population.[1,2] Moreover, it was suggested that veterans initiating ESRD with a Veterans Affairs (VA) healthcare provider may have better survival, and a lower probability of initiating at a higher eGFR, compared to those initiating with a non-VA provider.[1,2,18] Finally, a study investigating solely eGFR slope in the veteran population showed that a rapid decline was associated with higher long-term post-ERSD mortality.[19]

However, no study has examined whether veterans who transition to ESRD with both a lower eGFR and a less progressive disease, have better or worse early post-ESRD outcomes.

We sought to examine these outcomes in a contemporary cohort of US veteran patients transitioning to ESRD and hypothesized that the combination of a slower disease progression and lower kidney function level upon transition is associated with better immediate post-ESRD outcomes.

Methods

Study Population and Data Source

We retrospectively analyzed data from the Transition-of-Care-in-CKD study, which investigates veterans transitioning to ESRD between October 1, 2007 and March 30, 2014.[1] The source population comprised 85,505 veterans identified from the USRDS. We excluded 1958 patients for missing follow-up information, 32,280 patients with missing data on VA measured serum creatinine, and 29,724 with no available creatinine measurement within 31 days prior to transition. To calculate eGFR slope using a mixed effects regression model during the 12 months prior to ESRD, we further required that these patients have at least two eGFR measurements (including a measure within 31 days before transition) and over 30 days apart. After excluding patients without these criteria, and slope outliers at 0.5 and 99.5 percentiles, our final cohort comprised 19,985 veterans with both 31-day measured pre-ESRD (prelude) eGFR and 12-month prelude eGFR slope (Supplemental Figure 1).

This study was approved by the Institutional Review Boards of the Memphis and Long Beach Veterans Affairs Medical Centers. Due to the large sample size, patient anonymity, and nonintrusive nature of the research, the written consent requirement was exempt.

Demographic, Clinical and Laboratory Measurements

Data from three national databases: USRDS, VA and Centers for Medicare and Medicaid Services (CMS) were combined to determine baseline characteristics. Marital status was obtained from VA records. Receipt of pre-ESRD care was obtained from USRDS records of the CMS 2728 Medical Evidence Form. Pre-existing comorbidity information was extracted from VA and CMS datasets using International Classification of Diseases, Ninth Revision (ICD-9) Diagnostic and Current Procedural Terminology codes. Charlson comorbidity index was calculated without renal disease. Presence of a comorbidity was assigned using a one inpatient or two outpatient visits algorithm.

Prelude laboratory measurements were sourced from VA databases only. Data on serum creatinine and other laboratory measurments were obtained from the VA Corporate Data Warehouse LabChem and Decision Support System National Data Extracts Laboratory Results files, respectively. Data on body mass index (BMI) and blood pressure were obtained from the VA Corporate Data Warehouse Vital Signs file. The closest measurement to transition within 31 days prelude period was used in analyses as baseline values.

Exposure Measurement

The primary exposure was the combination of 31-day prelude eGFR and rate of kidney function change in the 12-month prelude period. eGFR was calculated with the Chronic Kidney Disease Epidemiology Collaboration equation.[20] Based on the approximate median

of the cohort and previous studies,[11,12,19] eGFR was dichotomized as: <10 and ≥10 mL/min/1.73m^2 to represent low and high eGFR at transition, respectively. Disease progression (slope) was calculated using mixed effects linear regression to ascertain the annual eGFR slope prior to transition. Based on the approximate median of the cohort and prior study,[19] slopes were dichotomized as: >−10 and ≤−10 mL/min/1.73m^2/year to represent slow and fast eGFR slope, respectively. A total of four combined groups (2×2) were created as our primary exposure, with a low 31-day eGFR and a slow 12-month eGFR slope group as the reference.

Outcome Assessment

The outcomes of interest were 12-month all-cause mortality, 12-month cardiovascular (CV) mortality, and 12-month hospitalization rate after transition. Cardiovascular reasons for death were obtained from the USRDS. Data on all-cause events, including death and hospitalizations were sourced from VA, CMS and USRDS datasets. Patients were followed from the start of ESRD until death, kidney transplantation, lost to follow-up, end of the 12-month follow-up period, or September 2, 2014, whichever occurred first. For CV mortality, the last date of follow-up was June 30, 2014.

Statistical Analysis

Baseline patient characteristics were described as proportion, mean ± standard deviation or median [interquartile range, IQR], and differences across eGFR groups were compared with tests of chi-square, ANOVA or Kruskal-Wallis, where appropriate.

Predictors of a low eGFR and slow slope (reference= all other kidney profiles), higher eGFR (reference= low eGFR), and faster disease progression (reference= slow slope) were examined using logistic regression.

The relationship of the combination of eGFR and slope with 12-month all-cause or CV mortality was examined using Cox proportional hazard models. To evaluate the association of the combined eGFR and slope groups with 12-month hospitalization incidence rate, Poisson and negative binomial regression models were used.

For each outcome, three models of adjustment were used: (i) unadjusted model; (ii) case-mix adjusted model that included the time interval between the last eGFR measurement and transition date, age, gender, race, ethnicity, incidence year, marital status, Charlson comorbidity index, diabetes, ischemic heart disease (ISHD), myocardial infarction, congestive heart failure (CHF), cerebrovascular disease and chronic obstructive pulmonary disease (COPD); and (iii) case-mix+MICS (malnutrition-inflammation cachexia syndrome) adjusted model which included case-mix model variables and baseline measurements of bicarbonate, blood urea nitrogen (BUN), hemoglobin, albumin, phosphorus, calcium, potassium, BMI, and systolic and diastolic blood pressure.

Sensitivity Analyses

We conducted sensitivity analyses to examine the robustness of the observed associations. The eGFR and slope-mortality association was evaluated across strata of clinical

characteristics. Wald tests for interaction were performed in the fully adjusted models. As fluctuations in eGFR may occur, a subgroup of 5285 patients were excluded if hospitalized within the 12-month prelude period with a primary diagnosis of an acute kidney injury (AKI) (ICD-9 code 584 or 586), or were indicated as recovered renal function by the USRDS within 60 days from transition.

Next, we examined additional categorizations of combined eGFR and slope. We examined granular groups guided by approximate quartiles of the cohort. A total of 16 groups were created, representing eGFR (<7, 7-<10, 10-<13 and ≥13 mL/min/1.73m^2) and slope (>−5, −5->−10,−10−>−15, and ≤−15 mL/min/1.73m^2/year).

Additionally, we also calculated percentile ranks (value 1–100) for eGFR and slope, respectively. A low percentile would represent a lower eGFR or slower slope, and a high percentile would represent a higher eGFR or faster slope. These percentiles were summed together (eGFR percentile plus slope percentile) or subtracted from each other (eGFR percentile minus slope percentile) and their respective association with all-cause mortality was evaluated using restricted cubic splines.

Finally, we calculated propensity scores to account for patient differences. For propensity score models, we examined associations of: 1) eGFR and included eGFR slope as a covariate and 2) eGFR slope with eGFR as a covariate. We used the propensity score in multiple analyses, including the propensity score in covariate adjustment, stratification based on propensity score tertiles, and finally, matching by propensity score.[21]

Data for demographics was missing for <0.15% and were imputed using a missing category. Laboratory variables were missing on average 11% and were imputed by means. Analyses were conducted using SAS Enterprise Guide (7.1) (Cary, NC), and Stata/MP Version 14 (College Station, TX).

Results

Baseline clinical characteristics stratified by eGFR and slope groups are presented in Table 1. The cohort was 66±11 years, and included 2% females and 34% blacks. The median [IQR] of eGFR at transition and slope was 9.7[7.1, 13.3] mL/min/1.73m^2 and −10.5[−18.8, −5.9] mL/min/1.73m^2/year, respectively. In our cohort, 26% of patients transitioned to ESRD with a low eGFR and slow slope and were more likely to be black, have pre-ESRD nephrology and dietician care, and had a lower prevalence of diabetes, depression, and COPD.

Predictors of a low eGFR and slow eGFR Slope

In adjusted analyses, compared to all other disease profiles, black race and higher albumin were associated with higher odds of initiating with a low eGFR and slow slope (OR[95%CI]: 1.51[1.39, 1.63] and 1.83[1.72, 1.96], respectively , Table 2). Conversely, in both unadjusted and fully adjusted models, presence of CHF was associated with lower odds of transitioning with a low eGFR and slow slope (OR[95%CI]: 0.60[0.56, 0.64] and 0.77[0.71, 0.84], respectively).

Predictors of a high eGFR or fast eGFR Slope

Among all patients who met eGFR criteria (n=21,543), presence of CHF consistently had the highest odds of transitioning with a high eGFR across all models (Supplemental Table 1A). Conversely, in the fully adjusted model, predictors of lower eGFR included female sex, black race, Hispanic ethnicity, cerebrovascular disease, and higher albumin, BUN, and phosphorus.

In our analytical cohort, predictors of a faster slope included higher eGFR, hospitalization at transition, Charlson comorbidity index, and COPD across all models (Supplemental Table 1B). Negative predictors of a faster slope included age, black race, ISHD, and higher hemoglobin. Higher albumin was associated with the lowest odds of a fast slope (OR [95%CI]: 0.49[0.46,0.52] after full adjustment).

Association of eGFR and Slope with 12-Month Mortality

Over a median follow-up of 366 days, 3945 deaths occurred, yielding a crude all-cause death rate of 23.1 per 100 patient-years [95%CI: 22.4, 23.8]. Patients with a low eGFR and slow slope had the lowest death rate of 13.8 per 100 patient-years [95%CI: 12.8, 14.9].

In unadjusted analyses, a low eGFR and slow slope was associated with the lowest risk of 12-month all-cause and CV mortality (Figure 1A and 1B). After additional levels of adjustments, this relationship still persisted, as a low eGFR and slow slope was associated with the lowest risk of 12-month all-cause and CV mortality, although slightly attenuated with CV mortality. The greatest eGFR and fastest slope was associated with the highest risks of 12-month all-cause and CV mortality (HR [95% CI]: 1.80 [1.62, 1.99] and 1.57 [1.32, 1.88], respectively in fully adjusted models) compared patients with a low eGFR and slow slope. Associations were similar in sensitivity analyses when excluding patients with an AKI or recovered function, and examining more granular groups. Patients with the highest eGFR at transition (≥13 mL/min/1.73m2), and fastest slope (≤−15 mL/min/1.73m2/year), had the highest risk of both 12-month all-cause and CV mortality across all levels of adjustment (Supplemental Table 2A and 2B).

Likewise, we observed that a low eGFR and slow slope was associated with lower mortality risk in the fully adjusted models across most strata of clinical characteristics, including race/ethnicity and BMI. The hazard ratios for eGFR and slope groups across most strata were similar to that of the association observed in all patients, further confirming the robustness of our observed results (Supplemental Figure 2). However, there was significant effect modification by initial modality (P-interaction=.03). Among initial peritoneal dialysis (PD) patients (<5%) with an aggressive disease profile we observed a 45% lower risk of mortality after fully adjustment though not significant (HR [95%CI]: 0.55[0.22, 1.37]). There was significant interaction in eGFR and slope groups with a number of comorbidities: diabetes, ISHD, MI, and CHF. Similar to that of the overall cohort, a low eGFR and slow slope was also associated with the lowest CV mortality risk across most subgroups (Supplemental Figure 3). However, many of the observed relationships across strata were largely attenuated due to a small number of events and sample size.

We also used the eGFR and slope composite sum or difference score to evaluate the combined effect. In summed rank variables, there was a linear association with 12-month all-cause mortality after full adjustment, where patients with a low eGFR and slow slope had the lowest risk for mortality (reference=100; Figure 2A). When examining the difference in percentile ranks, we observed a U-shaped association with 12-month all-cause mortality. Patients with either a low eGFR and fast slope, or high eGFR and slow slope had the highest adjusted risks of all-cause mortality compared to the reference of 0 (patients with either combination of low eGFR and slow slope, or high eGFR and fast slope) (Figure 2B).

Propensity Score Sensitivity Analyses

To account for characteristic differences, we calculated propensity scores of transitioning to ESRD with a high or low eGFR (Supplemental Table 3A). After matching, higher eGFR was associated with approximately 30% higher risk of 12-month all-cause mortality among 12,532 matched patients after across all levels of adjustment (Table 3A). Among the analytical cohort, additional propensity score analyses resulted in similar findings under all models. Likewise, we calculated propensity scores of transitioning to ESRD with a slow or fast eGFR slope (Supplemental Table 3B). In this matched cohort (n=16,482), a faster slope was associated with a higher risk of all-cause mortality (HR[95%CI]: 1.35[1.25, 1.45], Table 3B). Similar findings were observed in the full cohort with additional propensity scoreanalyses.

Association of eGFR and Slope and Hospitalization Rates

Finally, we examined the relationship of eGFR and slope with 12-month hospitalization incidence rate. Patients experienced a median [IQR] of 1[0, 3] hospitalizations over the early ESRD period. In all adjustments, we observed that a low eGFR and slow slope was associated with a lower hospitalization incidence rate (Figure 3). Similar to mortality analyses, patients with an aggressive disease profile had the highest 12-month hospitalization rate (IRR [95% CI]: 1.39[1.34, 1.44]) after full adjustment. The observed associations were similar in sensitivity analyses, including when modeled with negative binomial regression, excluding patients for an AKI or recovered function, and under more granular groups of eGFR at transition and slope (Supplemental Table 2C).

Discussion

In a contemporary cohort of 19,985 veterans who transitioned to ESRD, the combination of a lower kidney function with slower kidney disease progression, or low eGFR and slow slope, was associated with better early ESRD outcomes including lower all-cause and cardiovascular mortality risk and hospitalizations. The kidney disease profile of higher eGFR combined with fastest disease progression was associated with the highest risk of 12-month morbidity and mortality outcomes. These relationships remained robust in sensitivity analyses including propensity scores, which may mitigate the likelihood of selection bias upon transition to ESRD.

Previous studies investigating US population cohorts have primarily relied on eGFR at transition,[10–14] and have been limited in examining confounding due to nutritional status,[16]

especially from prior to transition, including slopes. Similar to past studies, we also observed higher mortality risk among patients with higher eGFR at transition, but after additionally accounting for eGFR slope, nutritional parameters and propensity for earlier transition. Many studies have demonstrated higher mortality risk with eGFR slope in many populations, including the community, elderly and early stage CKD patients.[22–26] However, few studies have examined pre-ESRD eGFR trajectories and post-ESRD mortality.[19,27] O'Hare et al., showed that a catastrophic loss of eGFR was associated with the highest risk of 1-year all-cause mortality, yet not in longer periods of follow-up (2–5 years).[27] We observed similar findings, in that an aggressive kidney disease profile including a fast slope was associated with higher early mortality risk. Additionally, Sumida et al., examined the eGFR slope-mortality association, with effect modification by last eGFR prior to transition.[19] The authors found that among patients with a last eGFR≥10mL/min/1.73m^2, a rapid loss was not associated with higher mortality risk (reference: slow decline [< −5 mL/min/1.73m^2/year]). We, however, did observe lower early mortality risk for patients initiating with a low eGFR and slow slope. In addition to differences in reference groups, we evaluated early mortality, whereas Sumida et al., examined long-term follow-up (median: 2 years),[19] and it is possible that the eGFR slope-mortality association among patients with a high eGFR at transition may be impacted by time-varying dialysis treatment covariates[1,28] and thus mitigating the long-term mortality risk.

It has been suggested that early initiators may lose renal function faster compared to later initiators as a repercussion of dialysis treatment especially in the early months post-transition with thrice-weekly hemodialysis as compared to incremental hemodialysis.[11,29] Dialysis may more strongly effect early initiators, thereby more rapidly losing residual renal function, and experiencing inflammation, cachexia, and body mass loss, which have been noted as predictors of mortality risk among incident ESRD patients.[11,30–32] Furthermore, decline in kidney function may be an indicator for other underlying conditions including atherosclerosis, oxidative stress, malnutrition and other cardiovascular diseases, which can contribute to higher morbidity and mortality.[19]

The lowest mortality risk, observed in patients with a low eGFR and slow slopw, may actually be indicative of better pre-ESRD care. Indeed, 80% and 31% of these patients had pre-ESRD nephrology and dietician care, respectively, compared to markedly less in other groups. Similar to observed trends in a previous study,[27] the patients with a low eGFR and slow slope at initiation were less likely to initiate in a hospital and had fewer pre-ESRD hospitalizations. Thus, these patients may have had a better management of healthcare, including closer monitoring of disease progression and a planned, or maybe delayed transition at a lower eGFR level. These high levels of care may be carried through post-ESRD, such that these patients may less likely to be hospitalized and have a lower mortality risk after transition to ESRD. Thus together, both eGFR and disease progression in combination, are important risk factors in post-ESRD morbidity and mortality, and eGFR alone may no longer be a sole factor when transitioning to ESRD.[17,23] These data may have clinical and public health implications it suggests that a low eGFR and slow slope in the immediate prelude period is associated with more favorable early ESRD outcomes. It is suggestive that delaying transition until a lower eGFR among patients with either degree of slope may afford better outcomes, including a lesser life burden from time on dialysis.

This study should be qualified for several potential limitations. Due to the observational nature of the study design, residual confounding cannot be completely excluded, nor can causal relationship be implied. An inherent limitation is confounding by indication, where patients with a given eGFR at transition may have other symptoms that would prompt transition to ESRD. While we found similar associations in sensitivity analyses when excluding AKI patients, this may not completely capture patients as one needed to be primarily diagnosed with an AKI. Thus it is possible that late stage chronic kidney disease patients may have had an AKI event that went unnoticed, or not identified as a primary diagnosis. We adjusted for nutritional parameters which although did not strongly attenuate observed associations, it is possible that these markers are on the causal pathway and covariate inclusion may be over adjustment. We adjusted for available confounders; however markers of renal function such as iothalamate or iohexol clearances, or muscle mass were unavailable. We only included patients with a measured serum creatinine 31 days prior to ESRD transition and met slope criteria, representing a select group of veterans who may be a more frequent user of VA services, however less than 10% of patients were excluded for not meeting slope criteria. In addition, there is survivor bias, as patients may have died before reaching ESRD, and thus were not an incident ESRD patient. Finally, given the composition of the VA population (almost 95% male), these findings may not be externally valid to other populations. But, our study strengths include the use and availability of combined data from VA, USRDS and CMS records, including repeated laboratory measures, which has often been missing in cohort studies. Furthermore, we used the Chronic Kidney Disease Epidemiology Collaboration formula in our eGFR calculation opposed the Modification of Diet in Renal Disease Study formula. Studies have suggested that the latter equation does not accurately estimate eGFR, which may lead to “greater” eGFR during initiation.[12,33] Finally, we used a linear mixed-effects regression model when calculating eGFR slope which may be superior in estimating change,[34] compared to examining a change in percent or eGFR category.[17] To our knowledge, this is one of the largest studies to investigate both ESRD timing and disease progression with early ESRD mortality and morbidity in US veterans.

Conclusion

In conclusion, we observed that in veteran patients transitioning to ESRD, transitioning with a low eGFR and slow slope was associated with lower risk of 12-month mortality and hospitalization, and this relationship was independent of laboratory markers. This relationship remained consistent across numerous sensitivity analyses. Together, these results further support the notion that an early transition to dialysis may not be as beneficial as once thought and additional studies are warranted to clarify this relationship.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

AKI	Acute Kidney Injury
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CHF	Congestive Heart Failure
CKD	Chronic Kidney Disease
CMS	Centers for Medicare and Medicaid Services
COPD	Chronic Obstructive Pulmonary Disease
CV	cardiovascular
eGFR	estimated glomerular filtration rate
ESRD	end-stage renal disease
ICD-9	International Classification of Diseases, Ninth Revision
IQR	interquartile range
ISHD	Ischemic Heart Disease
MICS	malnutrition-inflammation cachexia syndrome
Prelude	Pre-ESRD
USRDS	United States Renal Data System
VA	Veterans Affairs

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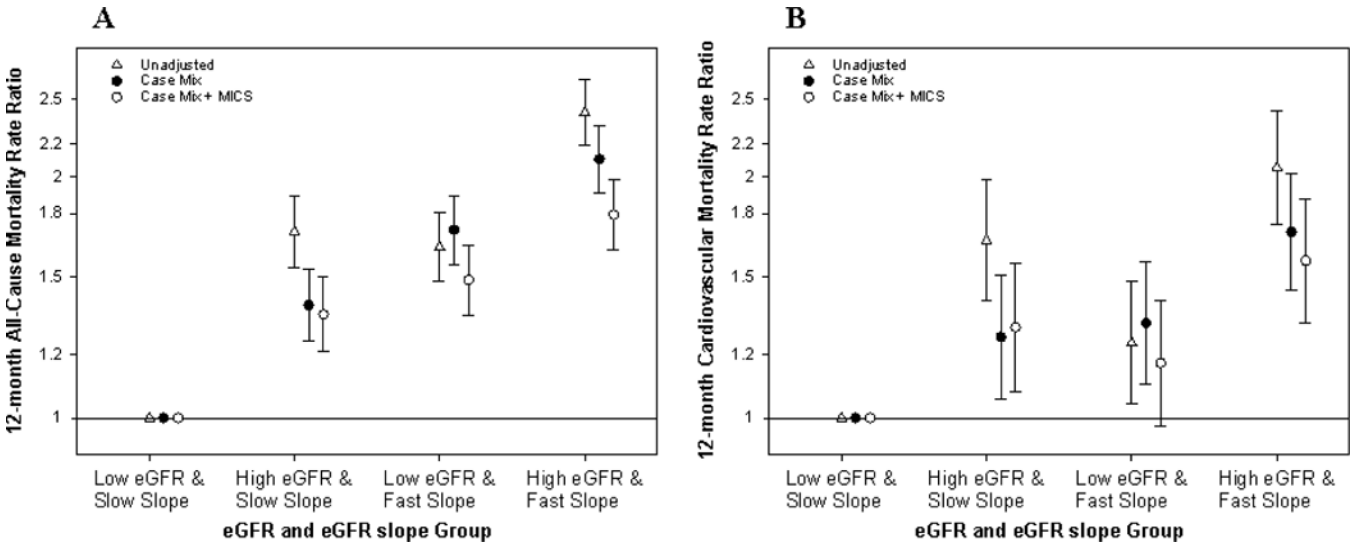

Figure 1.

Association of combined 31-day prelude eGFR and 12-month eGFR slope with 12-month A) all-cause mortality and b) cardiovascular mortality*

*eGFR; estimated glomerular filtration rate

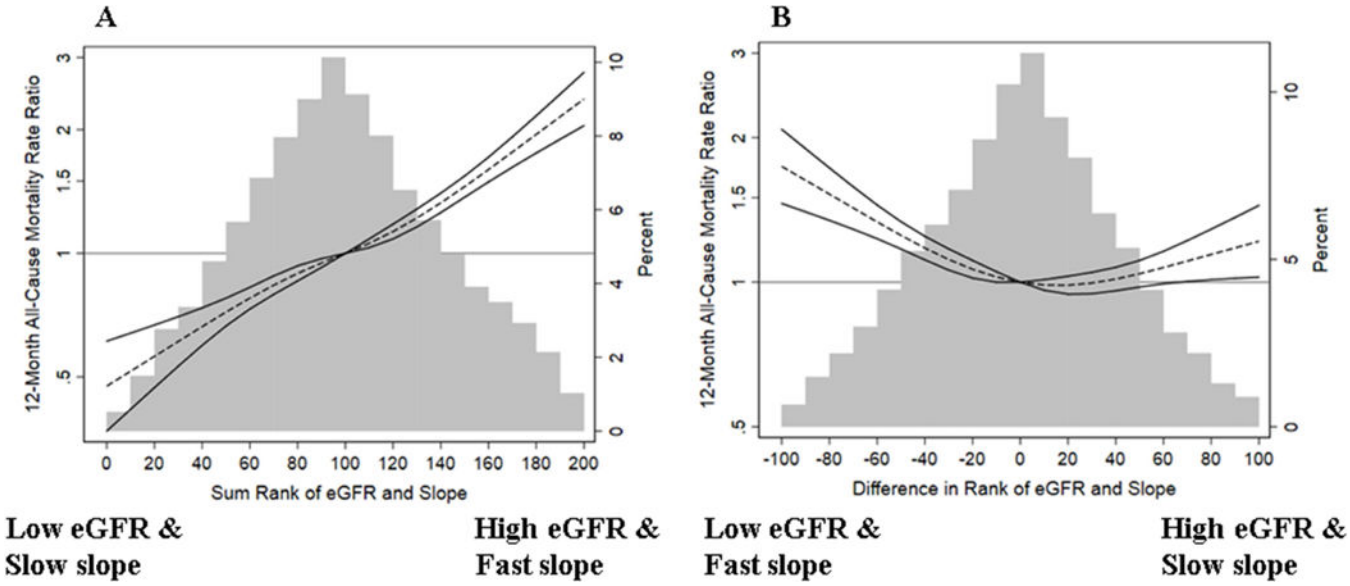

Figure 2.

Case-mix+MICS adjusted restricted cubic splines of the A)sum and B)difference in percentiles of eGFR and slope with 12-month all-cause mortality*

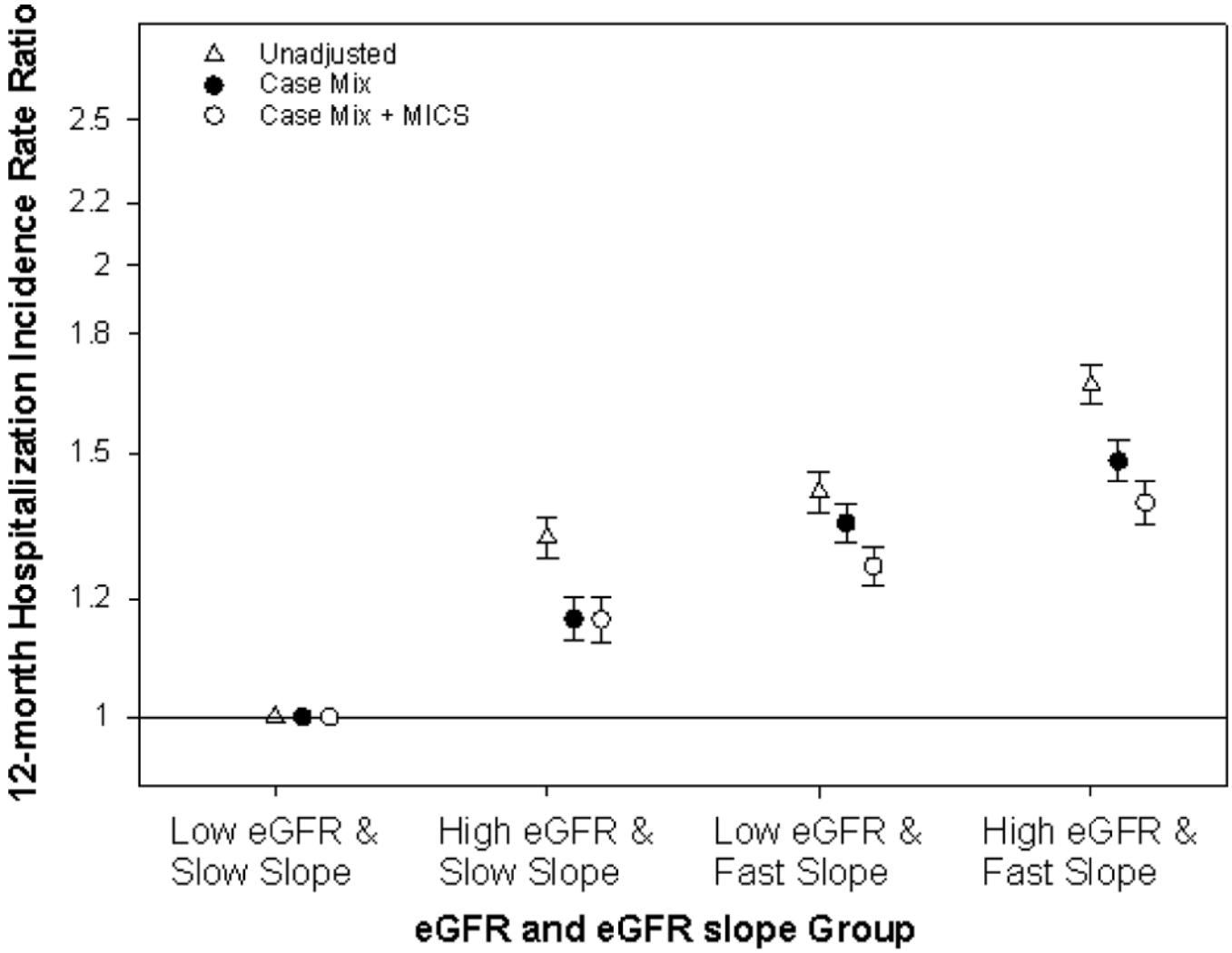

Figure 3.
Association of combined 31-day prelude eGFR and 12-month eGFR slope with 12- month Hospitalization Incidence Rate Ratio*

Table 1.

Baseline characteristics of 19,985 patients stratified by eGFR at transition and eGFR slope among veterans who transitioned to ESRD based on thresholds as eGFR 10 mL/min/1.73m^2 and eGFR slope of −10 mL/min/1.73m^2/year[a,b]

		eGFR at Transition and Slope			
	Total	**Low eGFR/ Slow Slope**	**High eGFR/ Slow Slope**	**Low eGFR/ Fast Slope**	**High eGFR/ Fast Slope**
N, %	19,985	5,204(26.0)	4,318 (21.6)	5,323(26.6)	5,140(25.7)
eGFR (mL/min/1.73 m^2)	9.7 [7.1,13.3]	7.3 [5.8,8.6]	13.2 [11.4,16.2]	7.2 [5.7,8.6]	14 [11.7,18.5]
eGFR slope (mL/min/1.73 m^2/year)	−10.5 [−18.8,−5.9]	−5.8 [−7.9,−3.8]	−5.6 [−7.7,−3.3]	−17.3 [−29,−12.9]	−19.1 [−31,−13.4]
Days between eGFR measurement and transition	−1[−9,0]	−−1[−8,0]	−3[−13,0]	0[−3,0]	−3[−14,0]
Age (years)	66±11	67±11	68±10	65±11	66±11
Gender (%)					
Female	2	3	2	3	2
Race (%)					
White	61	55	67	57	65
Black	34	39	29	37	29
Other	5	5	4	6	5
Ethnicity (%)					
Hispanic	8	9	7	9	8
Marital Status (%)					
Married	49	50	53	45	49
Hospitalization					
Initiated in Hospital	57	50	50	66	60
Count in 6 month prelude	1[0,2]	1[0,2]	1[1,2]	1[1,2]	2[1,3]
Pre-ESRD Care					
Nephrology	68	80	75	62	54
Dietician	25	31	27	23	18
Charlson comorbidity index	3[2,5]	3[2,4]	4[2,5]	3[2,5]	4[3,6]
Comorbidities (%)					
Diabetes	71	67	75	68	75
Anemia	69	76	76	61	65
Atrial Fibrillation	12	8	16	9	16
Depression	28	24	28	28	31
ISHD	50	44	60	41	56

		eGFR at Transition and Slope			
	Total	**Low eGFR/ Slow Slope**	**High eGFR/ Slow Slope**	**Low eGFR/ Fast Slope**	**High eGFR/ Fast Slope**
MI	19	15	25	15	24
CHF	48	38	57	40	57
PVD	32	27	37	27	36
Cerebrovascular Disease	25	23	30	23	27
Dementia	2	2	2	2	2
COPD	35	27	41	31	43
Paraplegia/Hemiplegia	3	2	3	3	3
Laboratory measurements in 31-day prelude					
CO_2 (mEq/L)	22.3±4.8	21±4.4	23.7±4.4	20.9±4.7	24±4.6
BUN(mg/dL)	73.9±30.9	86.1±27.9	62.9±26.3	84.1±30.4	60.3±28.9
Hemoglobin (g/dL) *	9.8±4.6	9.7±1.6	10.2±1.6	9.5±1.5	10.0±1.7
Albumin * (g/dL)	3.2±0.7	3.4±0.6	3.3±0.6	3.3±0.7	3.0±0.7
Phosphorus (mg/dL)	5.5±1.8	6.1±1.7	4.5±1.2	6.3±1.9	4.7±1.4
Calcium (mg/dL)	8.5±0.9	8.5±1	8.7±0.8	8.2±0.9	8.5±0.8
iPTH (pg/mL)	250 [138,415]	322 [147,526]	210 [124,338]	289 [167,464]	189 [108,313]
Potassium (mEq/L)	4.4±0.7	4.5±0.7	4.4±0.7	4.5±0.7	4.4±0.7
Weight (lbs)	204±51	201±47	204±52	204±51	207±53
Body Mass Index (kg/m^2)	29.9±6.9	29.4±6.5	29.9±7	29.7±6.8	30.3±7.3
Systolic BP (mmHg)	142±23	144±22	139±22	144±24	138±24
Diastolic BP (mmHg) *	74±14	74±14	71±12	76±14	73±14

[a] BP; blood pressure, BUN; blood urea nitrogen, CHF; congestive heart failure, COPD; chronic obstructive pulmonary disorder, CO_2; bicarbonate, eGFR; estimated glomerular filtration rate, iPTH; intact parathyroid hormone, ISHD; Ischemic Heart Disease; MI; myocardial infarction, PVD; peripheral vascular disease.

[b] Data presented as proportion, mean ± standard deviation or median [interquartile range] where appropriate. Data compared between eGFR & slope groups with tests for chi-square, ANOVA, or Kruskal-Wallis where appropriate. P-values for all variables were <0.01 except where noted with *.

Table 2.

Multivariable logistic regression based estimated odds ratios (OR) of a low eGFR and slow eGFR slope upon transition compared to all other eGFR and slope groups (reference)[a]

	Unadjusted	Case Mix	Case Mix + MICS
Characteristic	OR(95%CI)	OR(95%CI)	OR(95%CI)
Age (Δ10 years)	**1.06**(1.03,1.09)	**1.23**(1.19,1.27)	**1.21**(1.16,1.25)
Female	**1.22**(1.00,1.50)	**1.20**(0.97,1.49)	**1.42**(1.14,1.77)
Race (Ref. White)			
Black	**1.39**(1.30,1.49)	**1.45**(1.35,1.56)	**1.51**(1.39,1.63)
Other	**1.22**(1.05,1.4)	**1.20**(1.03,1.39)	**1.31**(1.12,1.53)
Ethnicity			
Hispanic	**1.18**(1.05,1.31)	**1.26**(1.12,1.42)	**1.29**(1.14,1.46)
Incidence Year	**1.05**(1.03,1.07)	**1.09**(1.04,1.14)	**1.10**(1.05,1.16)
Married	**1.04**(0.98,1.11)	**1.08**(1.01,1.15)	**1.04**(0.97,1.11)
Initiated in Hospital	**0.70**(0.66,0.74)	**0.72**(0.67,0.77)	**0.59**(0.55,0.64)
Comorbidities			
Charlson comorbidity index	**0.86**(0.85,0.88)	**0.89**(0.87,0.91)	**0.91**(0.88,0.93)
Diabetes	**0.76**(0.71,0.81)	**1.00**(0.92,1.08)	**0.95**(0.87,1.04)
ISHD	**0.72**(0.68,0.77)	**0.97**(0.89,1.05)	**1.00**(0.92,1.09)
MI	**0.66**(0.60,0.72)	**0.96**(0.86,1.06)	**0.96**(0.86,1.07)
CHF	**0.60**(0.56,0.64)	**0.77**(0.72,0.83)	**0.77**(0.71,0.84)
Cerebrovascular Disease	**0.83**(0.77,0.89)	**1.07**(0.99,1.17)	**1.10**(1.01,1.21)
COPD	**0.61**(0.57,0.65)	**0.80**(0.74,0.87)	**0.85**(0.78,0.93)
Laboratory Measures			
CO_2 (Δ1 mEq/L)	**0.92**(0.91,0.93)	**0.93**(0.92,0.93)	**0.96**(0.95,0.97)
BUN (Δ10 mg/dL)	**1.19**(1.17,1.2)	**1.20**(1.19,1.22)	**1.16**(1.14,1.17)
Hemoglobin (Δ1 g/dL)	**0.94**(0.92,0.96)	**0.95**(0.93,0.97)	**0.95**(0.93,0.98)
Albumin (Δ1 g/dL)	**1.85**(1.75,1.95)	**1.86**(1.76,1.97)	**1.83**(1.72,1.96)
Phosphorus (Δ1 mg/dL)	**1.26**(1.23,1.29)	**1.28**(1.25,1.31)	**1.16**(1.13,1.20)
Calcium (Δ1 mg/dL)	**1.06**(1.02,1.1)	**1.09**(1.05,1.13)	**1.11**(1.06,1.16)
Potassium (Δ1 mEq/L)	**1.24**(1.18,1.3)	**1.24**(1.18,1.29)	**1.00**(0.95,1.06)
Body Mass Index (Δ5 kg/m^2)	**0.94**(0.92,0.97)	**0.99**(0.96,1.02)	**0.99**(0.96,1.02)
Systolic BP (Δ10 mmHg)	**1.07**(1.06,1.09)	**1.05**(1.04,1.07)	**1.08**(1.05,1.10)
Diastolic BP (Δ10 mmHg)	**1.05**(1.03,1.08)	**1.01**(0.99,1.04)	**0.96**(0.93,1.00)

[a]BP; blood pressure, BUN; blood urea nitrogen, CHF; congestive heart failure, COPD; chronic obstructive pulmonary disorder, CO_2; bicarbonate, ISHD; Ischemic Heart Disease; MI; myocardial infarction

Table 3.

Propensity Score Analyses for matching, adjustment and tertile stratification for the association of A) high eGFR (ref: low eGFR) and B) fast eGFR Slope (ref: slow eGFR slope) with 12-month all-cause mortality

A)

Propensity Score Analyses		Unadjusted		Case Mix [a]		Case Mix +MICS [a]	
	N	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)
Matched	12532	<.001	1.38(1.27,1.49)	<.001	1.33(1.22,1.44)	<.001	1.33(1.23,1.44)
Adjusted for Propensity Score	19985	<.001	1.58(1.49,1.69)	<.001	1.29(1.20,1.39)	<.001	1.29(1.20,1.39)
Tertile 1	6596	<.001	1.66(1.44,1.91)	<.001	1.51(1.30,1.74)	<.001	1.50(1.29,1.74)
Tertile 2	6794	<.001	1.24(1.10,1.38)	<.001	1.24(1.10,1.39)	.002	1.20(1.07,1.35)
Tertile 3	6595	<.001	1.34(1.18,1.53)	<.001	1.34(1.18,1.52)	<.001	1.29(1.13,1.48)

Propensity Score Analyses		Unadjusted		Case Mix [b]		Case Mix +MICS [b]	
	N	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)
Matched	16482	<.001	1.36(1.27,1.46)	<.001	1.38(1.28,1.48)	<.001	1.35(1.25,1.45)
Adjusted for Propensity Score	19985	<.001	1.53(1.43,1.63)	<.001	1.34(1.25,1.43)	<.001	1.34(1.25,1.43)
Tertile 1	6596	<.001	1.58(1.39,1.79)	<.001	1.59(1.4,1.80)	<.001	1.54(1.36,1.75)
Tertile 2	6794	<.001	1.46(1.31,1.64)	<.001	1.46(1.30,1.63)	<.001	1.41(1.26,1.58)
Tertile 3	6595	.01	1.14(1.03,1.27)	.01	1.17(1.05,1.30)	.04	1.12(1.01,1.25)

[a] Adjusted models additionally include eGFR slope as a covariate

[b] Adjusted models additionally include eGFR as a covariate